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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,461	03/27/2001	Benjamin D. Silverman	YOR920000779US2	1831
7590 10/07/2005			EXAMINER	
Ryan, Mason & Lewis, LLP 1300 Post Road, Suite 205 Fairfield, CT 06430			BORIN, MICHAEL L	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 10/07/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/818,461

Applicant(s)

SILVERMAN, BENJAMIN D.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) \_\_\_\_\_ is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***DETAILED ACTION***

***Status of the claims***

1. Claims 1-43 are pending. Claims 4,7-21,28-32,36,39-43 remain withdrawn from consideration.

Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The specification is repeatedly objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, page 17. Applicant is requested to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01(b).

***Claim Rejections - 35 USC § 112, second paragraph.***

3. Claim 1, and claims dependent therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is "a method for spatially profiling proteins", however, the claim recites a final step of "shifting the hydrophobicity distribution". While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. The claim does not set forth the conditions when the determining/shifting of hydrophobicity distribution results in "spatially profiling proteins".

Response to arguments

Applicant argues that the steps of determining hydrophobicity distribution are the steps of spatial profiling. By the way of example, applicant points at p.9. Apart from this example, however, specification teaches on p. 4, last paragraph, that hydrophobicity distribution is merely a "value that indicates the degree to which a residue is attracted or repelled by water". Therefore, Examiner reiterates that obtaining just a number characterizing a residue does not correspond to "spatial profiling", and thus maintains that the claim language fails to recite a final process step which agrees back with the preamble.

***Claim Rejections - 35 U.S.C. § 101***

4. Claims 1-3,5,6,22-24,26,27,33-35,37,38 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claims are directed to a method of shifting hydrophobicity distribution of a protein. The claims do not recite any particular result of such "shifting" or "spatial

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profiling" and do not recite any particular protein of interest for which such analysis would yield any identified useful information.

The Court of Customs and Patent Appeals has stated:

"Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." A "use" to do further research is not considered a utility which provides an "immediate benefit" to the public.

Examples of situations requiring further research to identify or reasonably confirm a "real world" context of use, and which do not have utility under 35 USC 101, as set forth in MPEP 2107.01.1, include:

(A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved,

and

(C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility.

The claimed invention seems to be drawn to basic research drawn to studying properties of a protein structure; as such it does not result in an "immediate benefit" to the public. The art in bioinformatics, as related to application of computational methods to analysis of protein structure, is highly unpredictable. Thus, with respect to applying parameters of hydrophobicity, Karplus (Protein Science, 6, 1997, p. 61302-61307) teaches (p. 1302, second paragraph) :

Over the years, numerous "hydrophobicity scales" and "solvation parameters" have been proposed based on both theoretical considerations and  $\Delta G$  transfer measurements...

Differences among such scales have fueled an active debate regarding which values, if any, are the ones that are relevant for protein folding, and led some to abandon the paradigm of hydrophobicity in favor of the more absolute concept of hydration

As noted in the utility guidelines (see: Federal Register, December 21, 1999, Volume 64, Number 244), basic research on a product to identify properties is an unsubstantial utility (see page 6 of the Utility guideline training materials). Therefore, the claims do not have substantial utility.

***Claim Rejections - 35 USC § 102 .***

5. Claims 1,3,6,22,24,27,33,35,38 are rejected under 35 U.S.C. 102(b) as anticipated by Cornette et al. (J. Mol. Biol., 1987,195,659-685).

Cornette teaches calculation of hydrophobic moment for each residue (*cf.* claim 6) - i.e., determining "hydrophobicity distribution" - and plotting them on a graph. See p. 660, right column through p. 661, left column, and Fig. 2. Fig. 2 presents "normalized intensity" i.e., values which are based on the "difference between values of hydrophobicity and average hydrophobicity. For comparative purposes, to compare different approaches, the hydrophobicity values are normalized (*cf.* claim 3) to have a value of 1000 at the frequency angle of 100° (i.e., "hydrophobicity distribution" is "shifted").

With respect to claims 22,24,27,33,35,38, the method of Cornette is computer-assisted and thus involves computer medium and computer system.

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claim are instantly disclosed by the teaching of the reference cited above.

**Response to arguments**

Applicant argues that amendment of the claim overcame the rejection. Examiner disagrees. Cornette, in Fig. 2 presents "normalized intensity" i.e., values which are based on the "difference between values of hydrophobicity and average hydrophobicity.

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6. Claims 1,3,6,22,24,27,33,35,38 are rejected under 35 U.S.C. 102(b) as anticipated by Eisenberg et al. Faraday Symposia of the Chemical Society, 1982, 17, 109-120.

Eisenberg et al describes determination of hydrophobicity distribution in proteins. To reconcile "hydrophobicity scales" from different publications which provide values of hydrophobicity for amino acid residues, Eisenberg "normalized" hydrophobicity. The scales were combined by averaging the normalized hydrophobicities for each residue over five scales, the result was multiplied by standard deviation and added to its mean. See p. 110 and Table 1. Therefore, the Eisenberg reference reads on the instantly claimed method comprising steps of shifting hydrophobicity distribution based on a difference between values in the hydrophobicity distribution and an average hydrophobicity value.

With respect to claims 22,24,27,33,35,38, the review article of Eisenberg does not specify the way calculations have been made. However, providing an automatic means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631

mlb  
09/22/2005